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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/765,466 | 01/26/2004 | Sachiko Machida | 690115.401C1 | 8356 |

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| EXAMINER | |
|---|---|
| YU, MELANIE J | |

| ART UNIT | PAPER NUMBER |
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| 1641 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/765,466 | MACHIDA ET AL. | |
| | Examiner | Art Unit | |
| | Melanie Yu | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,17,44 and 45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,17,44 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 29 October 2007 has been entered.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham **v.** John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

2. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Holtzman (US 5,969,123) in view of Schatz (US 5,932,433) further in view of Tall et al. (US 6,756,228).

Holtzman teaches a biochip for a screening assay (col. 12, lines 7-8) comprising a biotinylated receptor protein immobilized via a factor capable of specifically binding to biotin (streptavidin specifically binds to biotin and the biotinylated proteins is immobilized to the

streptavidin, col. 12, lines 8-16), wherein the receptor protein comprises a biotinylation sequence motif (biotinylated protein comprises biotinylation sequence motif, col. 12, lines 11-16), and wherein the receptor protein has the ability of being specifically bound by a ligand of the receptor protein (col. 8, line 65-col. 9, line 6). Holtzman fails to teach the biotinylation of the receptor protein carried out within a bacterial host and the receptor specifically being LOX-1.

Schatz teaches a recombinantly expressed biotinylated receptor protein immobilized via a factor capable of specifically binding to biotin (peptides are biotinylated and bound to streptavidin which specifically binds to biotin, col. 8, lines 10-27, biotinylated peptide may be a protein, col. 6, lines 13-19), wherein the receptor protein comprises a biotinylation sequence motif (when peptides are biotinylated, they gain a biotinylation sequence motif, col. 8, lines 10-27; col. 4, lines 57-60), wherein the biotinylation of the receptor protein has been carried out within a bacterial host instead of in vitro (carried out in *E. coli* host cells, col. 3, lines 47-50; col. 8, lines 10-14), in order to provide a protein that has been biotinylated.

Tall et al. teach a LOX-1 receptor immobilized to a substrate (col. 12, lines 29-38; col. 11, line 52-col. 12, line 57), in order to detect the presence of LOX-1 activity.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the biotinylation of the receptor protein of Holtzman, biotinylation in vivo instead of in vitro as taught by Schatz, in order to provide a simplified biotinylation process (Schatz, col. 2, lines 59-63). It would have further been obvious to one having ordinary skill in the art at the time the invention was made to include as the receptor protein of Holtzman in view of Schatz, a receptor protein of LOX-1 as taught by Tall et al., in order to provide a substrate that indicates a decreased or increased susceptibility to atherosclerosis. Although Holtzman in view of Schatz further in view of Tall

et al. fail to specifically teach the immobilized receptor protein obtained by refolding a biotinylated receptor protein expressed as an inclusion body within the host, such a limitation is drawn to a method of making the protein on the chip. The instant claims encompass a product of the receptor chip and not a method of making the product, the LOX-1 immobilized on the chip as taught by the prior art must be the same receptor protein required by the claims. Since the combination of prior art references described above, teaches a LOX-1 receptor protein biotinylated in a bacterial host and then immobilized on the substrate via the biotinylation sequence motif, the combination of the prior art references teaches the required structural limitations of the claim and the LOX-1 protein of the prior art reads on the claimed LOX-1 protein.

3. Claims 17 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brigham-Burke et al. (US 5,395,587) in view of Holtzman (US 5,969,123) further in view of Schatz (US 5,932,433) and Tall et al. (US 6,756,228).

Brigham-Burke et al. teach a protein immobilized on a SPR substrate (sensor chip, col. 5, lines 29-35; col. 5, lines 10-23) that conforms to a shape of an insertion site of a surface plasmon resonance device (sensor chip fits through a slot in the housing for SPR detection, 14, Fig. 1; col. 5, lines 30-35), but fail to teach the protein being biotinylated and immobilized via a factor capable of binding specifically to biotin.

Holtzman in view of Schatz further in view of Tall et al., as applied to claim 1, teach a biotinylated receptor protein immobilized on a substrate via a factor capable of specifically binding to biotin, in order to provide immobilization of receptor proteins on a substrate.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include on the substrate of Brigham-Burke et al., an immobilization technique of a biotinylated receptor protein as taught by Holtzman in view of

Schatz further in view of Tall et al., in order to simple and efficient immobilization of proteins on a substrate.

4. Claims 17 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muramatsu (Piezoelectric Crystal Biosensor Modified with Protein A for Determination of Immunoglobulins, 1987, Analytical Chemistry, vol. 59, pages 2760-2763) in view of Holtzman (US 5,969,123) further in view of Schatz (US 5,932,433) and Tall et al. (US 6,756,228).

Muramatsu teaches a protein immobilized on a crystal oscillator (pg. 2760, right column, last paragraph), but fail to teach the protein being biotinylated and immobilized via a factor capable of binding specifically to biotin.

Holtzman in view of Schatz further in view of Tall et al., as applied to claim 1, teach a biotinylated receptor protein immobilized on a substrate via a factor capable of specifically binding to biotin, in order to provide immobilization of receptor proteins on a substrate.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include on the substrate of Muramatsu, biotinylation of a protein receptor and immobilization via a factor capable of binding specifically to biotin as taught by Holtzman in view of Schatz further in view of Tall et al., in order to simple and efficient immobilization of proteins on a substrate.

***Response to Arguments***

5. Applicant's arguments filed 29 October 2007 have been fully considered but they are not persuasive. Applicant argues that the combination of Holtzman, Schatz and Tall et al. fail to teach a receptor protein of LOX-1 that has the ability of being specifically bound by a ligand of the receptor protein. At page 7, applicant argues that according to Kataoka et al., a LOX-1 protein must be modified with necessary sugar chains in order to retain ligand binding, which is not taught by Holtzman, Schatz or Tall et al. Applicant's argument is not

persuasive because applicant has not shown that the protein resulting from the biotinylation of Holtzman in view of Schatz further in view of Tall et al. is not capable of binding to a ligand. The claims do not specify to which ligand the receptor protein is capable of binding. The ligand of Holtzman in view of Schatz further in view of Tall et al. has the ability of binding to an antibody expressed against the LOX-1 protein biotinylated within a bacterial host. Additionally, Kataoka et al. teach that a deglycosylated LOX-1 merely exhibits reduced affinity for Ox-LDL binding (see abstract, last 2 sentences), which indicates that while the binding to the natural ligand may not be optimal, the receptor protein that has not been modified with sugar chains is capable of binding to its ligand.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melanie Yu whose telephone number is (571) 272-2933. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Melanie Yu
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